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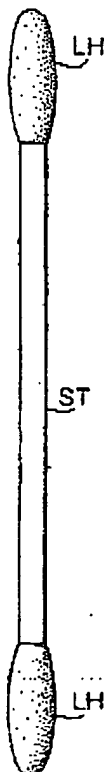
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IE, IL, KE, LK, LS, MN, MW, MZ, NZ, OM, SD, SG, SL,  
SZ, TT, TZ, UG, ZA, ZM, ZW only): UNILEVER PLC  
[GB/GB]; Unilever House, Blackfriars, London, Greater  
London EC4P 4BQ (GB).(71) Applicant (for IN only): HINDUSTAN LEVER LTD.  
[IN/IN]; Hindustan Lever House, 165 - 166 Backbay Rec-  
lamation, Mumbai 400 020 (IN).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BECK, Jonathan,  
Samuel [GB/GB]; Unilever Research Port Sunlight,  
Quarry Road East, Bebington, Wirral, Merseyside CH63  
3JW (GB). BLYTH, Simon, James [GB/GB]; Unilever  
Research Port Sunlight, Quarry Road East, Bebington,  
Wirral, Merseyside CH63 3JW (GB). BIJLANI, Nand,

[Continued on next page]

(54) Title: APPLICATOR

(57) Abstract: Pre-dosed applicator for applying a benefit agent, selected from the group consisting of sensitive  
teeth agent, anti-caries agent, anti-tar agents, fresh breath agents, vitamins, flavours, plaque disclosing agents  
and mixtures thereof, to teeth.

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Sanmukdas [IN/IN]; D/5, Mira Mansion, Sion Circle, Bombay 400 022 (IN). KETKAR, Vaidehi, Maneesh [IN/IN]; Hindustan Lever Ltd., Research Centre, Chakala, Mumbai 400 099, Andheri East (IN). MALONE, Siobhán, Louise [GB/GB]; Unilever Research Port Sunlight, Quarry Road East, Bebington, Wirral, Merseyside CH63 3JW (GB). NAVADA, Rekha [IN/IN]; Hindustan Lever Ltd., Research Centre, Chakala, Mumbai 400 099, Andheri East (IN).

(74) Agent: ROSEN JACOBSON, Frans, L., M.; Unilever NV, Patent Department, Olivier van Noortlaan 120, NL-3133 AT Vlaardingen (NL).

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APPLICATOR

The present invention relates to a pre-dosed applicator with a benefit agent that ensures localised application of the agent to the target area while ensuring minimal contact with other oral tissues.

Dental plaque is a non-mineralised microbial accumulation that adheres tenaciously to tooth surfaces. It is composed of an organic matrix derived from salivary glycoproteins and extracellular microbial products and cannot be removed by rinsing or water spray. It is common to all human populations, and if not regularly and thoroughly removed by proper brushing and allowed to accumulate on tooth surfaces, can lead to dental disease.

Plaque is translucent or tooth coloured and hence not easily visible, therefore an individual is frequently not aware of plaque itself as well as the quantity and location in the mouth. One way for effective plaque control is to make a person aware of what plaque is and its effects on the surrounding tissues. This can be done by visually demonstrating plaque on one's teeth which would show the person that he/she does have bacterial deposits on teeth which might cause future damage and therefore cause concern and hence motivation for practising good oral hygiene. Using dye indicators known as plaque disclosing agents does this visual demonstrating of plaque.

Disclosing agents that are currently available are organic dyes such as erythrosin dyes, fluorescent synthetic dyes

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which are invisible to the naked eye under normal daylight and only become visible by using light of proper wavelength, two tone dyes which differentiate between new and old plaque etc. Further typical disclosing agents include tartrazine  
5 yellow; patent Blue V; crystal violet; ruthenium red; 5-cyano-2, 3-ditolyltetrazolium chloride; amaranth; FDC Red 40; congo red; rosaniline; neutral red; safranin; FDC red 3; FDC blue 1; FDC green 3; Hercules green shade 3; fluorescein; red betamine; and yellow vulgaxanthine.

10

Conventional methods of applying these disclosing agents are either as a solution or as disclosing tablets. These methods have the disadvantages in that there is non-discriminatory staining of gingival tissues and lips and the colour remains  
15 on the tissue surfaces even after rinsing and disappears gradually. This is one factor that prevents people from using disclosing agents routinely.

US4992256 (Colgate-Palmolive Co., 1991) teaches aqueous,  
20 aerosol spray, chewing gum, wafer and tablet form of active ingredient-FD & C red no.3 to detect dental plaque by naked eye under visible light conditions.

US4431628 (Colgate-Palmolive Co., 1984) discloses a natural  
25 red dye from sugar beets formulated as a solution, tablet, gel, powder or aerosol for selectively staining said plaque formation on tooth surfaces without staining the adjacent oral tissues.

30 Other forms of the product such as chewable tablet, wafer, powder, lozenges, aerosol, liquid concentrate are also known

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where various known plaque disclosing actives have been incorporated.

However, there is no effective teaching for selective  
5 application of the plaque disclosing agent on the teeth for the purpose without staining the neighbouring oral soft tissue and lips.

It has now been possible to dispense selective amounts of  
10 the plaque disclosing agent using an applicator on the teeth by which the plaque, pellicle, germs and bacteria is selectively stained without staining the neighbouring oral soft tissue and lips. This applicator is more effective than the commonly used method of application of dye by disclosing  
15 tablets or solution. It is convenient to use and is very economical.

Thus according to a first aspect the invention provides an applicator for a benefit agent, which applicator comprises a  
20 means for entraining said benefit agent in a liquid form, said means being liquid absorbable. Preferably, said benefit agent is selected from the group consisting of sensitive teeth agents, anti-carries agents, anti-tartar agents, fresh breath agents, vitamins, flavours, plaque disclosing agents  
25 and mixtures thereof.

A device according to the invention thus provides the consumer with a means for specifically targeting an area of the oral cavity without using a large amount of said agent.  
30 It also provides the consumer with a means for specifically targeting an area needing attention. The prior art only

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being able to provide means for targeting the oral cavity as a whole.

The antimicrobial agents, which may provide an anti-tartar or anti gingivitis effect include: Triclosan, chlorhexidine, copper-, zinc- and stannous salts such as zinc citrate, zinc sulphate, zinc glycinate, sodium zinc citrate and stannous pyrophosphate, sanguinarine extract, metronidazole, quaternary ammonium compounds, such as cetylpyridinium chloride; bis-guanides, such as chlorhexidine digluconate, hexetidine, octenidine, alexidine; and halogenated bisphenolic compounds, such as 2,2' methylenebis-(4-chloro-6-bromophenol); anti-inflammatory agents such as ibuprofen, flurbiprofen, aspirin, indomethacin etc.

Anti-carries agents such as sodium- and stannous fluoride, aminefluorides, sodium monofluorophosphate, sodium trimeta phosphate and casein.

The benefit agent according to the invention may also comprise any of the following ingredients:

plaque buffers such as urea, calcium lactate, calcium glycerophosphate and strontium polyacrylates;

vitamins such as Vitamins A, C and E; plant extracts;

desensitising agents, e.g. potassium citrate, potassium chloride, potassium tartrate, potassium bicarbonate,

potassium oxalate, potassium nitrate and strontium salts;

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anti-calculus agents, e.g. alkali-metal pyrophosphates,  
hypophosphite-containing polymers, organic phosphonates and  
phosphocitrates etc.;

5 biomolecules, e.g. bacteriocins, antibodies, enzymes, etc.;

flavours, e.g. peppermint and spearmint oils;

proteinaceous materials such as collagen;

10

preservatives;

opacifying agents;

15 colouring agents;

pH-adjusting agents;

sweetening agents;

20

pharmaceutically acceptable carriers, e.g. starch, sucrose,  
water or water/alcohol systems etc.;

surfactants, such as anionic, nonionic, cationic and

25 zwitterionic or amphoteric surfactants;

particulate abrasive materials such as silicas, aluminas,  
calcium carbonates, dicalciumphosphates, calcium  
pyrophosphates, hydroxyapatites, trimetaphosphates,

30

insoluble hexametaphosphates and so on, including  
agglomerated particulate abrasive materials, usually in

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amounts between 3 and 60% by weight of the oral care composition.

humectants such as glycerol, sorbitol, propyleneglycol,  
5 xylitol, lactitol etc.;

binders and thickeners such as sodium carboxymethyl-cellulose, xanthan gum, gum arabic etc. as well as synthetic polymers such as polyacrylates and carboxyvinyl polymers  
10 such as Carbopol®;

polymeric compounds which can enhance the delivery of active ingredients such as antimicrobial agents can also be included. Examples of such polymers are copolymers of  
15 polyvinylmethylether with maleic anhydride and other similar delivery enhancing polymers, e.g. those described in DE-A-3,942,643 (Colgate); and

20 buffers and salts to buffer the pH and ionic strength of the oral care composition.

Preferably the benefit agent is present in an amount capable of providing the necessary benefit. However, this may be far short of the required level necessary in a toothpaste to  
25 achieve the same effect. Accordingly, the device according to the invention comprises the benefit agent is a level ranging from 0.0001 to 1%, preferably from 0.001 to 0.5% of the weight of the liquid absorbable part of the device after application of the agent. Alternatively, the agent is  
30 present in an amount ranging from 0.01 to 1%, preferably from 0.02 to 0.7% by weight of the liquid which is applied



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to the liquid absorbable part of the head before storage either as a dried device or a wet device which is suitably sealed.

5 According to a preferred aspect of the invention there is provided an applicator wherein a liquid absorbable material loaded with the benefit agent is provided on at least one end of the applicator and the said liquid absorbable material is preferably moistened prior to contacting the applicator onto  
10 the natural or artificial oral prostheses.

The benefit agent may be in liquid form or even dried form so that it can be stored more easily. Dried applicators can be wetted immediately prior to use. Wet applicators may be  
15 stored in a sealed package so maintain freshness for use.

According to a preferred aspect the present invention provides a single or multiple use applicator capable of dispensing the required amount of plaque disclosing agent on  
20 to the natural or artificial oral prostheses.

According to another preferred aspect of the invention the applicator is provided with a liquid absorbable material that is loaded with the plaque disclosing agent in the  
25 liquid/solution form and is subsequently dried. It is particularly preferred that the drying is done by vacuum drying.

The different plaque disclosing agents that may be used for  
30 the purpose of the invention are mercurochrome, bismark

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brown, erythrosin, fast green, fluorescein, two tone dye and basic fuschin, the most preferred agent being erythrosin.

Preferred dyes include a combination of dyes such that a  
5 blue colour is obtained before the product has been used.  
Consumers prefer a blue colour to a red colour in devices  
such as those according to the invention. It is also  
advantageous to have a dye which actually changes colour on  
contact with plaque in the oral cavity such that there can  
10 be no mistake that the use of the product merely results in  
a transfer of dye. Preferably, the colour change results in  
a change from blue or green to pink.

A preferable combination of dyes includes a combination of  
15 FDC Red No. 3 and FDC Blue No. 3. Preferably the ratio of  
the red to blue ranges from 150:1 to 1:15, more preferably  
from 50:1 to 1:5 and especially preferably from 8:1 to 1:1.  
The amount of FDC Red No. 3 ranges from 0.1 to 1.5% by  
weight of the dye applied to the device, more preferably  
20 from 0.3 to 1.5% and most preferably from 0.6 to 1.3%. The  
amount of FDC Blue No. 3 ranges from 0.01 to 1.8% by weight  
of the dye applied to the device, more preferably from 0.05  
to 1.0% and most preferably from 0.1 to 0.5%. FDC Green No.  
3 may also be used in this combination of dyes.

25

The applicator may be designed for single or multiple use.  
The tip of the applicator is suitably sized and shaped to  
enable the use specifically on the teeth. It may vary in  
diameter from 1 mm To 10 mm, preferably from 2 mm to 8 mm  
30 and especially preferably from 2 mm to 6 mm. The head may be  
shaped circular, elliptical, tear drop shaped, conical,

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discoid, pear shaped, semicircular. When designed for multiple use there is provided a reservoir of the plaque disclosing agent such that the same may be made available for use on the oral prostheses as and when desired. The  
5 reservoir may be provided with the plaque disclosing agent in the solid or liquid form.

In single use applicators a known and required quantity is provided as a part of the liquid absorbable material on the  
10 applicator. For one application on the entire set of teeth the quantity of the dye required would be in the range 1mg to 10mg and preferably 1mg to 5mg. The tablet generally contains 12mg of the dye, a substantial amount of which gets wasted as the surrounding oral soft tissue also gets  
15 stained.

The liquid absorbable material may be made of natural or synthetic material and may be chosen from cotton, sponge, or cloth or any absorbent material. Preferably, it also  
20 comprise an abrasive substance such as chalk, silica, perlite, pumice or any other commonly used oral care abrasive.

The applicator is dried after the plaque disclosing agent is  
25 loaded on to the liquid absorbable part of the applicator by any suitable means and preferably by vacuum drying. The drying time is variable and may range from 3 to 4 hours and the temperature during drying may range from 60-80 degree Centigrade.

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The applicator may be packed suitably as single or multiple units.

If we reduce the quantity it may not be sufficiently  
5 available to stain the teeth and hence a certain amount of  
over dosing becomes essential which however, leads to the  
other problem of soft tissue staining. The applicator will  
preferentially be used on the teeth and thus the quantity of  
the material used is appropriate.

10 In a further aspect the applicator according to the  
invention may also be part of a kit comprising an oral care  
product in addition to the applicator. In such a kit the  
user benefits from whiter teeth, fresher breath, reduced  
15 caries, reduced plaque build up and reduced gingivitis  
because of the motivational benefit of having the applicator  
in the same package as the oral care product. The oral care  
product can be a toothpaste, mouthwash, gel, powder or any  
other form of an oral care product commonly used in the art.

20 The invention will now be illustrated by the following non-  
limiting examples.

Examples:

25

Description and preparation of the applicator:

Fig 1a and Fig 1b describes the single use applicator. In  
Fig 2a and Fig 2b, various other forms and shapes are  
30 disclosed. In Fig 1a and Fig 1b, there is shaft (ST) that  
has a liquid absorbable head (LH) at one end as in Fig 1a

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and at both ends as in Fig 1b. A reservoir is provided to enable multiple use. The liquid absorbable head was made of cotton and was loaded with 0.2ml of 2% erythrosin dye. The applicator was dried under vacuum for 3 hours at 80°C.

5

Figure 3 is an applicator according to the invention which comprises as well as a liquid absorbable head (LH) and a shaft (ST) there is a finger hose (FS) enabling a finger to be inserted such that application can be made using a single  
10 finger. In this way the device can be used in the more hard to reach areas of the mouth.

Figure 4 is an applicator according to the invention which has a reservoir (R) which stores the liquid to be applied.  
15 In this way multiple use may be catered for.

Figure 5 is an applicator comprising a shaft (ST) a liquid absorbable head (LH) and a toothpick. The toothpick in this case is at the end opposite the liquid absorbable head  
20 although this is not strictly necessary, albeit preferred.

#### Combination dyes

The bud is kept in contact with first dye FDC RED for 1  
25 minute. This is followed by second dye FDC BLUE for 1 minute. The bud is then dried at 90 ° C for one hour.

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FDC Red No.3	FDC Blue No.3	Colour on bud	Disclosing colour (Pink?)
0.3%	0.3%	VIOLET	OK
0.2%	0.25%	DARK BLUE	OK
0.3%	0.2%	BLUE-VIOLET	OK
0.5%	0.25%	BLUE	OK
0.6%	0.2%	BLUE	GOOD
1.25%	0.2%	BLUE-GREEN	GOOD
1.25%	0.4%	GREEN-BLACK	OK

#### CONCLUSIONS

5

The bud colour was blue obtained by the combination of 0.6% FDC RED with 0.2% FDC BLUE .The colour obtained on application was blue and the plaque disclosed was pink.

- 10 The plaque disclosing was found to be the best using 1.25% FDC RED with 0.2% FDC BLUE. The colour of the bud was bluish green colour.

#### Testing of the efficiency of the applicator:

15

- A panel of trained volunteers was divided into two groups. One group was asked to use the applicator and the other to chew a erythrosin containing tablet before the first brushing for the day. The applicator having the loaded liquid absorbable head containing erythrosin at both ends were provided. The panellists were asked to moisten one end of the applicator and move it along the surface of the teeth
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viewing the same in front of a mirror for about a minute.  
The presence of the plaque is visible immediately. The  
tablet also revealed the plaque if any on the teeth. The  
panellists were asked to brush their teeth with a dentifrice  
5 and a brush as routine. At the end of brushing and rinsing  
the mouth with water the other end of the applicator was  
similarly used to disclose the plaque if any.

There was minimal or no stain on the oral soft tissue when  
10 the applicator according to the invention was used but a  
deep red stain was visible when the tablet containing  
erythrosin was chewed and it lasted for about 2 hours.  
However, disclosure of the plaque on the teeth guided the  
brushing operation in both cases to the same extent.

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CLAIMS

1. Applicator for applying a benefit agent to teeth, said  
5 applicator comprising a handle and a liquid absorbable  
part.
2. Applicator according to claim 1, wherein the benefit  
agent is selected from the group consisting of sensitive  
10 teeth agents, anti-caries agents, anti-tartar agents,  
fresh breath agents, vitamins, flavours, plaque  
disclosing agents and mixtures thereof.
3. Applicator according to claim 1 or 2, wherein the  
benefit agent is a plaque disclosing agent.  
15
4. Applicator according to claim 1, wherein the applicator  
comprises a handle and an applicator head, the head  
comprising a liquid absorbable material for absorbing a  
20 plaque disclosing solution.
5. Applicator according to claim 3 comprising a dried  
plaque disclosing material in the applicator head.
6. Use of an applicator according to any of claims 1, 3 or  
25 4 applying plaque disclosing material to the teeth by  
first wetting the device and then applying to the teeth.



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Fig.1a.

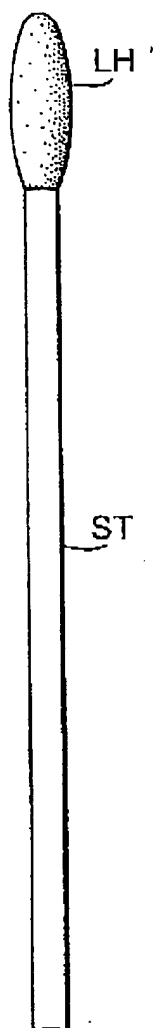
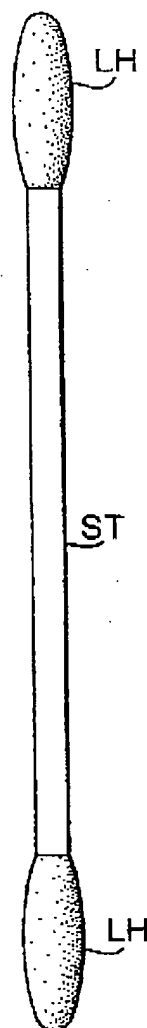


Fig.1b.

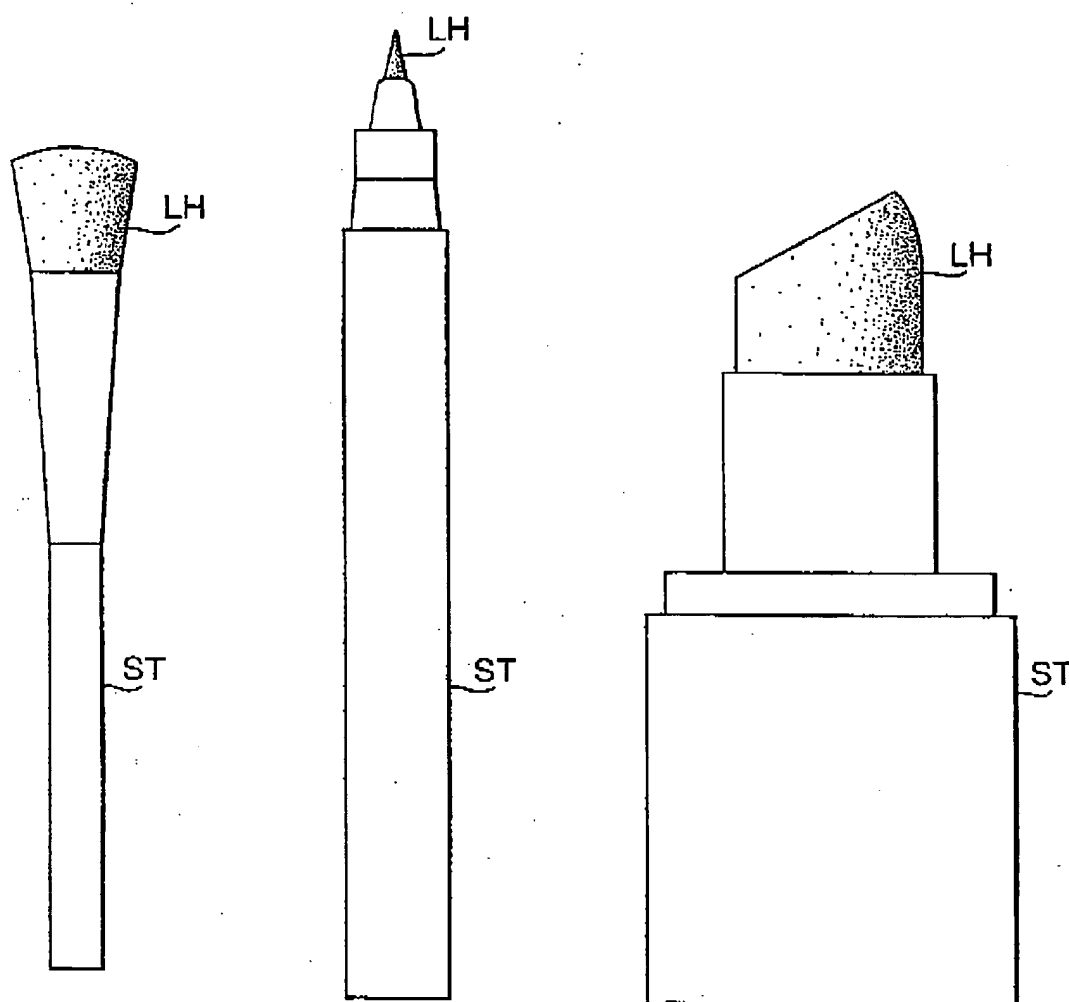


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Fig.2a.



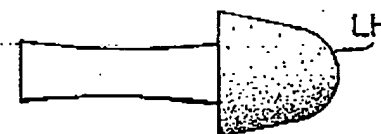
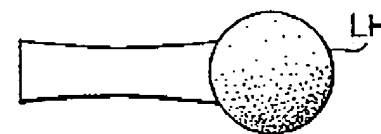
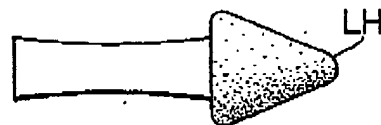
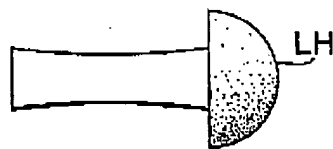
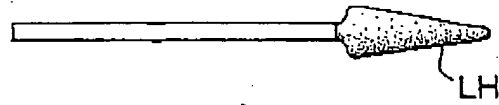
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Fig.2b.



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Fig.3a.

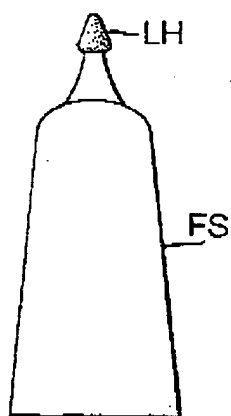


Fig.3b.

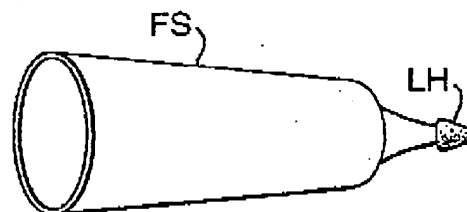
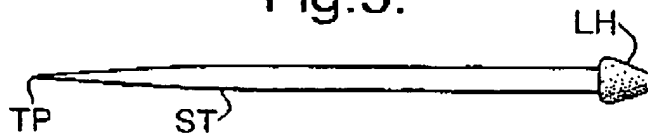


Fig.4.



Fig.5.



## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 02/03413A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61C19/06 A61M35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61C A61M A61K A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 947 986 A (LEWIS DARRIN R) 7 September 1999 (1999-09-07) abstract; figures column 3, line 13 -column 5, line 45	1,2,4
Y		3,5
X	EP 0 357 261 A (GAM MED PACKAGING CORP) 7 March 1990 (1990-03-07) column 6, line 16 -column 6, line 23; figures	1,2,4
X	US 5 846 215 A (ZYGOMT JOSEPH FRANK) 8 December 1998 (1998-12-08) column 1, line 35 -column 1, line 52; figures	1,4
	-/-	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel (+31-70) 340-2040, Tx. 31 651 epo nl  
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Fouquet, M

## INTERNATIONAL SEARCH REPORT

International Application No  
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C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 989 205 A (POND GARY J ET AL) 23 November 1999 (1999-11-23) the whole document	1,2,4
X	US 6 186 792 B1 (DISCKO JOHN J) 13 February 2001 (2001-02-13) abstract; figures	1,4
Y	US 4 431 628 A (GAFFAR MARIA C S) 14 February 1984 (1984-02-14) cited in the application abstract column 3, line 7 -column 3, line 50 column 4, line 26 -column 4, line 32 column 5, line 40 -column 5, line 59 column 7, line 27 -column 7, line 43	3,5

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 02/03413**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 6  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/EP 02/03413

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5947986	A	07-09-1999	NONE	
EP 0357261	A	07-03-1990	US 4952204 A AT 116561 T CA 1319907 A1 DE 68920382 D1 EP 0357261 A1 JP 2082972 A	28-08-1990 15-01-1995 06-07-1993 16-02-1995 07-03-1990 23-03-1990
US 5846215	A	08-12-1998	DE 19856629 A1 US 5919152 A	17-06-1999 06-07-1999
US 5989205	A	23-11-1999	NONE	
US 6186792	B1	13-02-2001	US 6049934 A BR 9803496 A EP 0903115 A2 JP 11151258 A	18-04-2000 09-11-1999 24-03-1999 08-06-1999
US 4431628	A	14-02-1984	NONE	